PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference .2521330 KSEH/RBR	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/AU2004/001423	International filing date *(day/month/year)* 15 October 2004	Priority date *(day/month/year)* 15 October 2003

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] C12N 15/48, A61K 39/21

Applicant

VIRAX DEVELOPMENT PTY LTD et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of 9 sheets, as follows:
      - [ ] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[X]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[ ]	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
15 August 2005	23 August 2005
Name and mailing address of the IPEA/AU	Authorized Officer
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/001423

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1 (b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☒ the description:

pages **1 - 45** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☒ the claims:

pages as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **46 - 54** received by this Authority on **15 August 2005** with the letter of 15 August 2005.
pages* received by this Authority on with the letter of

☒ the drawings:

pages **1/28 – 28/28** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 – 62.	YES
	Claims		NO
Inventive step (IS)	Claims	1 – 62.	YES
	Claims		NO
Industrial applicability (IA)	Claims	1 – 62.	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Citations

D1 WO 2000/028003 A1
D2 KENT, S. J., et. al. Vaccine 18:2250-6.
D3 WO 2004/058278 A1
D4 Chemical Abstracts 141:151863.

Novelty (N) and Inventive Step (IS)

The citations may disclose the treatment of retroviral infection by administering certain vectors to induce, enhance an immune response, but none of the citations D1 – D4 discloses or suggests methods of reducing or alleviating one or more side effects of anti-retroviral drug therapy in the manner presently claimed. Neither do the citations disclose or suggest certain vectors when used during interrupted antiviral drug therapy to prevent, reduce or delay viral rebound; or certain vectors when used to reduce or alleviate one or more side effects of antiviral drug therapy. Therefore the claimed matter is both novel and inventive.

Industrial Applicability (IA)

The claimed matter appears to be industrially applicable.

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
P,X WO 2004/058278	15 July 2004	15 December 2003	16 December 2002

The citation discloses the preparation of poxvirus vectors (particularly vaccinia) expressing IL-15 and viral peptides (particularly HIV peptides). See example 2 and Figure 5. The citation however does not disclose methods of reducing or alleviating one or more side effects of anti-retroviral drug therapy in the manner presently claimed.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/001423

Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material
      - [X] a sequence listing
      - [ ] table(s) related to the sequence listing

   b. format of material
      - [X] in written format
      - [ ] in computer readable form

   c. time of filing/furnishing
      - [X] contained in the international application as filed
      - [ ] filed together with the international application in computer readable form
      - [ ] furnished subsequently to this Authority for the purposes of search and/or examination
      - [ ] received by this Authority as an amendment* on

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Claims

1. A method of reducing or alleviating one or more side effects of anti-retroviral drug therapy comprising administering to a subject a poxvirus vector encoding an antigen of the retrovirus or the retrovirus antigen and a cytokine, or a functional homolog, derivative, part or analog of the retrovirus antigen and/or the cytokine, in conjunction with interrupted anti-retroviral drug therapy wherein the antigen or the antigen and the cytokine are expressed in the subject and are effective in maintaining or prolonging a low retroviral load in the subject for a period of time and are effective in preventing, reducing or delaying viral rebound during interruption of anti-retroviral drug treatment.

2. The method of claim 1, wherein the retroviral infection is HIV infection.

3. The method of claim 1 or 2, wherein the vector is administered to a subject exhibiting a low retroviral viral load as a result of anti-retroviral drug therapy.

4. The method of claim 1 or 2, wherein the vector is administered to a subject exhibiting a low retroviral load prior to commencement of anti-retroviral drug therapy.

5. The method of claim 1, 2, 3 or 4, wherein the cytokine is selected from IFNγ, IL-12, IL-2, TNF and IL-6.

6. The method of claim 5, wherein the cytokine is IFNγ.

7. The method of any one of claims 1 to 6, wherein the retrovirus antigen is encoded by a coding region selected from *gag, env, pol* and *pro* coding regions.

8. The method of claim 7, wherein the retrovirus antigen is encoded by *gag* and/or *pol* coding regions.

9. The method of claim 8, wherein the retrovirus antigen is encoded by *gag* and *pol* coding regions of HIV.

10. The method of any one of claims 1 to 9, wherein the poxvirus vector is an avipox virus vector.

11. The method of claim 10, wherein the avipox virus vector is a fowlpox virus vector.

12. A method for reducing or alleviating one or more side effects of anti-HIV drug therapy comprising administering to a subject a poxvirus vector comprising a sequence of nucleotides encoding a retrovirus antigen and a sequence of nucleotides encoding a cytokine, or a functional homolog, part, derivative or analog of the antigen and/or the cytokine, in conjunction with interrupted anti-retroviral drug therapy, wherein said method is effective in maintaining a low retroviral load in the subject and preventing, reducing or delaying retroviral rebound in the absence of anti-retroviral drug therapy.

13. The method of claim 12, wherein the retrovirus antigen is an HIV antigen.

14. The method of claim 12 or 13, wherein the vector is administered to a subject exhibiting a low retroviral viral load as a result of anti-retroviral drug therapy.

15. The method of claim 12 or 13, wherein the vector is administered to a subject exhibiting a low retroviral load prior to commencement of anti-retroviral drug therapy.

16. The method of claim 12, 13, 14 or 15, wherein the cytokine is selected from IFNγ, IL-12, IL-2, TNF and IL-6.

17. The method of claim 16, wherein the cytokine is IFNγ.

18. The method of claim 17, wherein IFNγ comprises the amino acid sequence set forth in SEQ ID NO: 6 or an amino acid sequence having at least about 60% similarity thereto.

19. The method of claim 17, wherein IFNγ is encoded by a sequence of nucleotides set forth in SEQ ID NO: 5 or a sequence of nucleotides encoding a functional homolog, part, derivative or analog thereof having at least 60% similarity thereto, or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency.

20. The method of any one of claims 12 to 19, wherein the retrovirus antigen is encoded by a coding region selected from *gag, env, pol* and *pro* coding regions.

21. The method of claim 20, wherein the retrovirus antigen is encoded by *gag* and/or *pol* coding regions.

22. The method of claim 21, wherein the retrovirus antigen is encoded by *gag* and *pol* coding regions of HIV.

23. The method of claim 22, wherein the retrovirus antigens encoded by *gag* and *pol* comprise the amino acid sequence set forth in SEQ ID NO: 2 or a functional homolog, part or derivative thereof or a sequence of amino acids having at least 60% similarity thereto, and SEQ ID NO: 4 or a functional homolog, part or derivative thereof, or a sequence of amino acids having at least 60% similarity thereto, respectively.

24. The method of claim 22, wherein the retrovirus antigen encoded by *gag* is encoded by a sequence of nucleotides set forth in SEQ ID NO: 1 or a sequence of nucleotides encoding a functional homolog, part or derivative thereof having at least 60% similarity thereto after optimal alignment or a sequence which hybridises

thereto or to a complementary form thereof under conditions of medium stringency, and wherein the retrovirus antigen encoded by *pol* is encoded by a sequence of nucleotides set forth in SEQ ID NO: 3 or a sequence of nucleotides encoding a functional homolog, part or derivative thereof having at least 60% similarity thereto after optimal alignment or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency.

25. The method of any one of claims 12 to 24, wherein the poxvirus vector is an avipox virus vector.

26. The method of claim 25, wherein the avipox virus vector is a fowlpox virus vector.

27. The method of claim 26, wherein the insertion site in the fowlpox vector comprises the sequence of nucleotides set forth in SEQ ID NO: 7.

28. A method of reducing or alleviating one or more side effects of anti-retroviral drug therapy comprising administering to a subject exhibiting a retroviral infection a poxvirus vector comprising a sequence of nucleotides encoding an antigen of the retrovirus or a functional derivative, homolog, part or analog thereof, and a sequence of nucleotides encoding a cytokine or a functional derivative, homolog, part or analog thereof in conjunction with interrupted anti-retroviral drug therapy, for a time and under conditions sufficient to co-express the antigen and the cytokine and to reduce or alleviate one or more side effects of anti-retroviral drug therapy in the subject.

29. The method of claim 28, wherein the retroviral infection is HIV infection.

30. The method of claim 28 or 29, wherein the vector is administered to a subject exhibiting a low retroviral viral load as a result of anti-retroviral drug therapy.

31. The method of claim 28 or 29, wherein the vector is administered to a subject

exhibiting a low retroviral load prior to commencement of anti-retroviral drug therapy.

32. The method of claim 28, 29, 30 or 31, wherein the cytokine is selected from IFNγ, IL-12, IL-2, TNF and IL-6.

33. The method of claim 32, wherein the cytokine is IFNγ.

34. The method of claim 33, wherein the IFNγ comprises the amino acid sequence set forth in SEQ ID NO: 6 or an amino acid sequence having at least about 60% similarity thereto.

35. The method of claim 33, wherein IFNγ is encoded by a sequence of nucleotides set forth in SEQ ID NO: 5 or a sequence of nucleotides encoding a functional homolog or derivative thereof having at least 60% similarity thereto, or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency.

36. The method of any one of claims 28 to 35, wherein the retrovirus antigen is encoded by a coding region selected from *gag, env, pol* and *pro* coding regions.

37. The method of claim 36, wherein the retrovirus antigen is encoded by *gag* and/or *pol* coding regions.

38. The method of claim 37, wherein the retrovirus antigen is encoded by *gag* and *pol* coding regions of HIV.

39. The method of claim 38, wherein the retrovirus antigens encoded by *gag* and *pol* comprise the amino acid sequence set forth in SEQ ID NO: 2 or a functional homolog, part or derivative thereof, or a sequence of amino acids having at least 60% similarity thereto, and SEQ ID NO: 4 or a functional homolog, part or

derivative thereof, or a sequence of amino acids having at least 60% similarity thereto, respectively.

40. The method of claim 38, wherein the retrovirus antigen encoded by *gag* is encoded by a sequence of nucleotides set forth in SEQ ID NO: 1 or a sequence of nucleotides encoding a functional homolog, part or derivative thereof, having at least 60% similarity thereto after optimal alignment, or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency, and wherein the retrovirus antigen encoded by *pol* is encoded by a sequence of nucleotides set forth in SEQ ID NO: 3 or a sequence of nucleotides encoding a functional homolog, part or derivative thereof having at least 60% similarity thereto after optimal alignment, or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency.

41. The method of any one of claims 28 to 40, wherein the poxvirus vector is an avipox virus vector.

42. The method of claim 41, wherein the avipox virus vector is a fowlpox virus vector.

43. The method of claim 42, wherein the insertion site in the fowlpox vector comprises the sequence of nucleotides set forth in SEQ ID NO: 7.

44. A use of a recombinant vector comprising a sequence of nucleotides encoding a retrovirus antigen or a functional derivative, homolog, part or analog thereof, and a sequence of nucleotides encoding a cytokine or a functional derivative, homolog, part or analog thereof in the manufacture of a medicament for use in conjunction with interrupted anti-retroviral drug treatment in maintaining or prolonging a low retroviral load in a subject for a period of time, and in preventing, reducing or delaying viral rebound during interruption of anti-retroviral drug treatment.

45. A use of a recombinant vector comprising a sequence of nucleotides encoding a

retrovirus antigen or a functional derivative, homolog, part or analog thereof, and a sequence of nucleotides encoding a cytokine or a functional derivative, homolog, part or analog thereof, in the manufacture of a medicament for use in reducing or alleviating one or more side effects of anti-retroviral drug therapy.

46. A use according to claim 44 or 45, wherein the retrovirus is HIV.

47. A recombinant poxvirus vector comprising a sequence of nucleotides encoding a retrovirus antigen or a functional homolog, derivative, part or analog thereof, and a sequence of nucleotides encoding a cytokine or a functional homolog, derivative, part or analog thereof, when used in conjunction with interrupted anti-retroviral drug therapy to maintain or prolong a low retroviral load in a subject and to prevent, reduce or delay viral rebound during interruption of anti-retroviral drug treatment in a subject.

48. A recombinant poxvirus vector comprising a sequence of nucleotides encoding a retrovirus antigen or a functional homolog, derivative, part or analog thereof, and a sequence of nucleotides encoding a cytokine or a functional homolog, derivative, part or analog thereof, when used for reducing or alleviating one or more side effects of anti-retroviral drug therapy.

49. The recombinant poxvirus vector of claim 48, when used for maintaining or prolonging a low retroviral load in the subject during anti-retroviral treatment interruption and for reducing or alleviating one or more side effects of anti-retroviral drug therapy.

50. The recombinant poxvirus vector of claims 47, 48 or 49, wherein the retrovirus is HIV.

51. The recombinant vector of claims 47, 48, 49 or 50, wherein the cytokine is selected from IFNγ, IL-12, IL-2, TNF and IL-6.

52. The recombinant vector of claim 51, wherein the cytokine is IFNγ.

53. The recombinant vector of claim 52, wherein the IFNγ comprises the amino acid sequence set forth in SEQ ID NO: 6 or an amino acid sequence having at least about 60% similarity thereto.

54. The recombinant vector of claim 52, wherein IFNγ is encoded by a sequence of nucleotides set forth in SEQ ID NO: 5 or a sequence of nucleotides encoding a functional homolog or derivative thereof having at least 60% similarity thereto or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency.

55. The recombinant vector of any one of claims 47 to 54, wherein the retrovirus antigen is encoded by a coding region selected from *gag, env, pol* and *pro* coding regions.

56. The recombinant vector of claim 55, wherein the retrovirus antigen is encoded by *gag* and/or *pol* coding regions.

57. The recombinant vector of claim 56, wherein the retrovirus antigen is encoded by *gag* and *pol* coding regions of HIV.

58. The recombinant vector of claim 57, wherein the retrovirus antigens encoded by *gag* and *pol* comprise the amino acid sequence set forth in SEQ ID NO: 2 or a functional homolog, part or derivative thereof or a sequence of amino acids having at least 60% similarity thereto, and SEQ ID NO: 4 or a functional homolog, part or derivative thereof or a sequence of amino acids having at least 60% similarity thereto, respectively.

59. The recombinant vector of claim 57, wherein the retrovirus antigen encoded by *gag*

is encoded by a sequence of nucleotides set forth in SEQ ID NO: 1 or a sequence of nucleotides encoding a functional homolog, part or derivative thereof having at least 60% similarity thereto after optimal alignment or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency, and wherein the retrovirus antigen encoded by *pol* is encoded by a sequence of nucleotides set forth in SEQ ID NO: 3 or a sequence of nucleotides encoding a functional homolog, part or derivative thereof having at least 60% similarity thereto after optimal alignment or a sequence which hybridises thereto or to a complementary form thereof under conditions of medium stringency.

60. The recombinant vector of any one of claims 47 to 59, wherein the poxvirus vector is an avipox virus vector.

61. The recombinant vector of claim 60, wherein the avipox virus vector is a fowlpox virus vector.

62. The recombinant vector of claim 61, wherein the insertion site in the fowlpox vector comprises the sequence of nucleotides set forth in SEQ ID NO: 7.